Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Proof-of-Concept Study to Evaluate Efficacy and Safety of Treatment with CNTO 136 Administered Intravenously in Subjects with Active Lupus Nephritis

Summary

EudraCT number	2010-020968-38
Trial protocol	BE NL
Global end of trial date	25 September 2013

Results information

Result version number	v1
This version publication date	06 July 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	CNTO136LUN2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01273389
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Antwerpseweg 15-17, B-2340 Beerse, Belgium,
Public contact	Clinical Registry Group, Janssen Cilag International NV, +31 715242166, clinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Cilag International NV, +31 715242166, clinicaltrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy and safety of CNTO 136 (sirukumab) administered intravenously (IV) in subjects with active, International Society of Nephrology (ISN)/Renal Pathology Society (RPS) Class III and IV lupus nephritis (LN).

Protection of trial subjects:

A Data Review Committee (DRC) was established that was composed of Johnson & Johnson clinicians and statisticians who were independent of the study team. The DRC was available to assess unblinded safety data and to make recommendations regarding the study, if needed, upon study team recommendation. Safety was assessed by monitoring (adverse effects (AEs), (serious adverse effects (SAEs), , chemistry and hematology laboratory tests, lipid tests, vital signs, general physical examination and skin evaluations, concomitant medication review, (electrocardiogram (ECG) testing (heart rate, PR interval, QRS interval, QT interval, and QTc using QTcB and QTcF correction methods), pregnancy testing, infusion reactions, and antibodies to CNTO 136

Background therapy:

Subject was required to receive stable immunosuppression with mycophenolate mofetil (MMF) 1 to 3 g/day (or equivalent dose of mycophenolic acid/ mycophenolate sodium [MPA]) with/without corticosteroids up to prednisone equivalent of 20 mg/day, or azathioprine 1 to 3 mg/kg/day with/without corticosteroids up to prednisone equivalent of 20 mg/day. They were also to be on a stable regimen of angiotensin converting enzyme (ACE) inhibitors and/or angiotensin II receptor blockers (ARBs), unless they were previously intolerant to or had contraindication to ACE inhibitors and ARBs.

Evidence for comparator: -

Actual start date of recruitment	28 January 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Thailand: 6
Country: Number of subjects enrolled	United States: 9
Country: Number of subjects enrolled	Belgium: 3
Worldwide total number of subjects	25
EEA total number of subjects	5

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 28 January 2011 to 25 September 2013 in 18 centers.

Pre-assignment

Screening details:

An 8-week run-in period was used to establish the stability of baseline renal parameters prior to randomization and the first study agent administration. A total of 25 subjects were randomized and treated in the study: 21 subjects in the CNTO 136 group and 4 subjects in the placebo group.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received comparable volume of placebo matching with CNTO 136 as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received placebo (5% dextrose solution) matching with CNTO 136 as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24.

Arm title	CNTO 136

Arm description:

Subjects received CNTO 136, 10 milligram per kilogram of body weight (mg/kg) as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24.

Arm type	Experimental
Investigational medicinal product name	CNTO136
Investigational medicinal product code	
Other name	Sirukumab, fully human anti-IL-6 mAb
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received CNTO 136, 10 milligram per kilogram of body weight (mg/kg) as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24.

Number of subjects in period 1	Placebo	CNTO 136
Started	4	21
Completed	4	15
Not completed	0	6
Consent withdrawn by subject	-	1
Non Serious Adverse Event	-	3
Serious Adverse Events	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received comparable volume of placebo matching with CNTO 136 as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24	
Reporting group title	CNTO 136
Reporting group description:	
Subjects received CNTO 136, 10 milligram per kilogram of body weight (mg/kg) as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24.	

Reporting group values	Placebo	CNTO 136	Total
Number of subjects	4	21	25
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	21	25
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: Years			
arithmetic mean	37.8	30.6	
standard deviation	± 11.44	± 7.72	-
Title for Gender Units: subjects			
Female	4	17	21
Male	0	4	4

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received comparable volume of placebo matching with CNTO 136 as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24	
Reporting group title	CNTO 136
Reporting group description:	
Subjects received CNTO 136, 10 milligram per kilogram of body weight (mg/kg) as intravenous infusion on Week 0, 4, 8, 12, 16, 20, and 24.	
Subject analysis set title	Modified Intent-to-Treat (m-ITT) Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
m-ITT population included of all subjects who received at least 1 (partial or complete) dose of study agent and had baseline and at least 1 evaluable post baseline efficacy outcome measurement.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis population included all subjects who were randomized and received at least 1 dose of study agent.	

Primary: Percent Reduction From Baseline in Proteinuria at Week 24

End point title	Percent Reduction From Baseline in Proteinuria at Week 24[1]
End point description:	
Percent reduction from baseline in proteinuria measured by protein/creatinine (P/C) ratio in a 12 hour urine collection obtained at Week 24. A last observation carried forward (LOCF) procedure was used to impute missing values if a subject had data for at least one post baseline evaluation. A a negative percenatage reduction indicates an increase (worsening) in urine proteinuria.	
End point type	Primary
End point timeframe:	
Baseline to Week 24	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not reported for this endpoint as inferential analysis was not performed as planned.

End point values	Placebo	CNTO 136		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[2]	20[3]		
Units: Percentage of subjects				
median (full range (min-max))	-43.26 (-257.5 to 49.8)	0 (-490.5 to 90.9)		

Notes:

[2] - Modified Intent-to-Treat Analysis population

[3] - Modified Intent-to-Treat Analysis population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Reduction in Proteinuria by at least 50% From Baseline up to Week 24

End point title	Percentage of Subjects with Reduction in Proteinuria by at least 50% From Baseline up to Week 24

End point description:

The percentage of subjects with a reduction in in proteinuria by at least 50% from baseline at any time through Week 24 is reported.

End point type	Secondary

End point timeframe:

Baseline Up to Week 24

End point values	Placebo	CNTO 136		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[4]	20[5]		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 0)	20 (5.7 to 43.7)		

Notes:

[4] - Modified Intent-to-treat Analysis Population

[5] - Modified Intent-to-treat Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with a Meaningful Reduction in Proteinuria

End point title	Percentage of Subjects with a Meaningful Reduction in Proteinuria

End point description:

Percentage of Subjects with meaningful reduction of proteinuria at any time through Week 24 was recorded. Meaningful reduction in proteinuria was defined as P/C (protein/creatinine) ratio to ≤ 0.5 for nonnephrotic subjects (defined as subjects with P/C ratio ≤ 3.0 at baseline); or at least 50% reduction in P/C ratio and P/C ratio ≤ 3.0 for nephrotic subjects.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Placebo	CNTO 136		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[6]	20[7]		
Units: Percentage of Subjects				
number (confidence interval 95%)	0 (0 to 0)	15 (3.2 to 37.9)		

Notes:

[6] - Modified Intent-to-treat Analysis population

[7] - Modified Intent-to-treat Analysis population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with no Worsening in Glomerular Filtration Rate (GFR)

End point title	Percentage of Subjects with no Worsening in Glomerular Filtration Rate (GFR)

End point description:

It was measured as the Percentage of subjects with no worsening in GFR at any time through Week 24. No worsening in GFR was defined as ≤ 15% decrease from baseline GFR.

End point type	Secondary

End point timeframe:

Baseline up to week 24

End point values	Placebo	CNTO 136		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[8]	20[9]		
Units: Percentage of subjects				
number (not applicable)	75	45		

Notes:

[8] - Modified Intent-to-treat Analysis population

[9] - Modified Intent-to-treat Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Subject's Global Assessment of Disease Activity

End point title	Mean Change From Baseline in Subject's Global Assessment of Disease Activity

End point description:

The Subject's Global Assessment of Disease Activity will be recorded on a visual analogue scale (VAS) (0 to 10 cm). Where, 0 cm=no disease activity and 10 cm=worst possible disease activity. Here, "n" is the number of subjects analysed for this outcome measure at specific time point

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Placebo	CNTO 136		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[10]	20[11]		
Units: Percent Change				
arithmetic mean (standard deviation)				
Baseline (n=4, 20)	3.5 (± 1.19)	4.1 (± 2.46)		
Mean Change at Week 24 (n=4, 20)	-0.55 (± 1.928)	-0.79 (± 2.662)		

Notes:

[10] - m-ITT population

[11] - m-ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Physician's Global Assessment of Disease Activity

End point title	Mean Change From Baseline in Physician's Global Assessment of Disease Activity

End point description:

The Subject's Global Assessment of Disease Activity will be recorded on a visual analogue scale (VAS) (0 to 10 cm) where, 0 cm=no disease activity and 10 cm=worst possible disease activity. Here, "n" is the number of subjects analysed for this outcome measure at specific time point.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Placebo	CNTO 136		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[12]	20[13]		
Units: Percent Change				
arithmetic mean (standard deviation)				
Baseline (n=4, 20)	4.5 (± 2.25)	4.2 (± 2.59)		
Mean Change at Week 24 (n=4, 20)	-0.85 (± 0.995)	-1.12 (± 2.073)		

Notes:

[12] - m-ITT Population

[13] - m-ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Initial of study up to 16 weeks after the final administration of drug	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1
Reporting groups	
Reporting group title	CNTO 136 10 mg/kg
Reporting group description: CNTO 136 10 mg/kg administered intravenously	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	CNTO 136 10 mg/kg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 21 (47.62%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Lymphadenitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic Thrombocytopenic Purpura			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Lupus Nephritis			
subjects affected / exposed	4 / 21 (19.05%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster Disseminated			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Escherichia Urinary Tract Infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Haemophilus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-Ovarian Abscess			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	CNTO 136 10 mg/kg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 21 (95.24%)	4 / 4 (100.00%)	
Vascular disorders			
Diastolic Hypertension			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hypertension			

subjects affected / exposed	3 / 21 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	5	0	
General disorders and administration site conditions			
Generalised Oedema			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	3	0	
Pyrexia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Oedema Peripheral			
subjects affected / exposed	1 / 21 (4.76%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Rhinitis Allergic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Respiratory Tract Congestion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Investigations			
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Muscle Strain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Cardiac disorders			
Pericardial Disease			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 21 (19.05%)	0 / 4 (0.00%)	
occurrences (all)	6	0	
Somnolence			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Iron Deficiency Anaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Neutropenia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vertigo			

subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Haematotympanum			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Keratitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Eczema Eyelids			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Ascites			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Abdominal Wall Haematoma			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Enteritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vomiting			

subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Tongue Ulceration			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Dermatitis Allergic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Cutaneous Lupus Erythematosus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Butterfly Rash			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Photosensitivity Reaction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Solar Dermatitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

Telangiectasia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Lupus Nephritis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Chondritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Escherichia Bacteraemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Anal Abscess			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

Furuncle			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Herpes Zoster			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Oral Candidiasis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Otitis Media			
subjects affected / exposed	0 / 21 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Sepsis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	3 / 21 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	4	0	
Pharyngitis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Upper Respiratory Tract Infection			
subjects affected / exposed	7 / 21 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	8	1	
Urinary Tract Infection			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	

Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Hyperlipidaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2011	It involved extension in time frame from 3 months to approximately 6 months prior to screening for having a renal biopsy showing active nephritis as one of the possible criteria to characterize subjects as having persistently active LN (lupus nephritis); clarification to the SLEDAI-2K (systemic lupus erythematosus disease activity index 2000) and the SRI-50 (systemic lupus erythematosus disease activity index 2000 (SLEDAI-2K) responder index-50) assessments; clarifications to the urine sample collection and analysis process; clarification to the proteinuria requirement criteria; clarification to the footnotes for the antibodies to CNTO 136 and CNTO 136 concentration samples; clarification to include an option for subjects to receive the equivalent immunosuppressant therapy mycophenolic acid/ mycophenolate sodium (MPA) instead of MMF; clarification to the timing with assessments and dosage administration.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported